REMARKS

Claims 28, 29, 35, 37, 38, 40 – 51 and 53 – 58 are pending. Claims 28, 29, 48, 49 and 57 have been amended. Claims 1 - 27, 30 – 34, 36, 39 and 52 were cancelled. No new claims have been added. No new matter has been added by virtue of the amendments, support being found throughout the specification and claims as originally filed.

Any cancellation of the claims should in no way be construed as acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Objections

The Examiner has objected to claim 28, line 10 and claim 29, line 12, for minor informalities. Applicants have corrected the claims and respectfully request that the objection be withdrawn. (Office Action, p.2).

35 U.S.C. §112, second paragraph

The Examiner has rejected claims 28, 29, 35, 37, 38, 41 – 50 and 52 – 58 under 35 U.S.C. §112, second paragraph, as being indefinite. (Office Action, p.2). The Examiner argues that "(c)laims 28, 29, 48, 49 and 57 recite the limitation "a substantially separate aqueous stream" is unclear as to whether the streams are separate or not." (Office Action, p.2). Applicants respectfully traverse the rejection.

Without acquiescing to any validity of the Examiner's rejection, and solely in the interest of advancing prosecution, Applicant's have amended the claims to delete the term "substantially."

Applicants point out page 12, line 6, of the present disclosure that defines "substantially separate aqueous stream" to refer to collimated streams with laminar flow

Accordingly, the claims are definite as written. Applicants respectfully request that the foregoing rejection be withdrawn.

35 U.S.C. §103(a)

Claims 28, 29, 38, 40, 48, 49, 51, 52, 53 and 56 were rejected under 35 U.S.C. 103(a) as being anticipated by Benavides et al. (US 6,443,179; the '179 reference herein) in view of Orwar et al. (6,455,303; the '303 reference herein). Applicants respectfully traverse the rejection.

Claims 35 and 58 were rejected under 35 U.S.C. 103(a) as being anticipated by Benavides et al. (US 6,443,179; the '179 reference herein) in view of Orwar et al. (the '303 reference), and further in view of Pfost et al. (5,104,621; the '621 reference herein). Applicants respectfully traverse the rejection.

Claims 41 - 43 were rejected under 35 U.S.C. 103(a) as being anticipated by Benavides et al. (US 6,443,179; the '179 reference herein) in view of Orwar et al. (the '303 reference),and further in view of Bjornson et al. (6,103,199; the '199 reference herein). Applicants respectfully traverse the rejection.

Claims 44, 45, 49 and 50 were rejected under 35 U.S.C. 103(a) as being anticipated by Benavides et al. (US 6,443,179; the '179 reference herein) in view Orwar et al. (the '303 reference), and further in view of Crandall et al. (6,352,766; the '766 reference herein). Applicants respectfully traverse the rejection.

Claims 46 and 47 were rejected under 35 U.S.C. 103(a) as being anticipated by Benavides et al. (US 6,443,179; the '179 reference herein) in view of Orwar et al. (the '303 reference), and further in view of DiZio et al. (6,455,152; the '152 reference herein). Applicants respectfully traverse the rejection.

Claims 54 and 55 were rejected under 35 U.S.C. 103(a) as being anticipated by Benavides et al. (US 6,443,179; the '179 reference herein) in view of Orwar et al. (the '303 reference), and further in view of Chiu et al. (7,470,518; the '518 reference herein). Applicants respectfully traverse the rejection.

Claims 54 and 55 were rejected under 35 U.S.C. 103(a) as being anticipated by Benavides et al. (US 6,443,179; the '179 reference herein) in view of Orwar et al. (the '303

reference), and further in view of Stanto et al. (7,125,660; the '660 reference herein). Applicants respectfully traverse the rejection.

Because all of the foregoing rejections rely on Benavides et al. (the '179 reference) and Orwar et al. (the '303 reference) in combination with other secondary references, and in the interest of more compact prosecution, Applicants will address the rejections under 35 U.S.C. 103(a) together.

The present claims recite a system comprising a macroscale device which is interfaced with a microfluidic device using double-sided tape to form a stable association between the microfluidic device and the macroscale device, wherein the double sided tape comprises a first adhesive surface which associates with the macroscale device and a second adhesive surface which associates with the microfluidic device, wherein the microfluidic device has three or more interdigitating microchannels suitable for containing a fluid stream; and at least one sensor chamber containing at least one sensor, and wherein each microchannel comprises an outlet for delivering a separate aqueous stream into the sensor chamber, wherein the outlets of the microchannels intersect with at least one of the sensor chambers, and wherein the microfluic device comprises a scanning mechanism for selectively exposing a sensor to multiple fluid streams from the three or more microchannel outlets. (Claim 28).

The claims also recite a system comprising a macroscale device which is interfaced with a microfluidic device using transfer tape to form a stable association between the microfluidic device having three or more microchannels comprising a fluid stream, and the macroscale device, wherein the transfer tape comprises a backing to which an adhesive surface is separably attached and wherein a bond between the adhesive and the backing is weaker than a bond between the adhesive and the macroscale or microfluidic surface, wherein the microfluidic device has three or more interdigitating microchannels suitable for containing a fluid stream, and wherein the microfluidic device has at least one sensor chamber containing at least one sensor, and wherein each microchannel comprises an outlet for delivering a separate aqueous stream into the sensor chamber, and wherein the outlets of the microchannels intersect with at least one of the sensor chambers, and

wherein the microfluic device comprises a scanning mechanism for selectively exposing a sensor to multiple fluid streams from the plurality of microchannel outlets. (Claim 29).

The '179 reference does not anticipate the invention as claimed. In particular, the '179 reference nowhere teaches or suggests a microfluidic device, let alone a system, as claimed, where the system comprises a macroscale device which is interfaced with a microfluidic device wherein **the microfluidic device has three of more interdigitating microchannels suitable for containing a fluid stream; and at least one sensor chamber containing at least one sensor, and wherein each microchannel comprises an outlet for delivering a separate aqueous stream into the sensor chamber, wherein the outlets of the microchannels intersect with at least one of the sensor chambers, and wherein the microfluic device comprises a scanning mechanism for selectively exposing a sensor to multiple fluid streams from the three or more microchannel outlets.**

The Examiner refers to Figure 21 and argues that the '179 reference teaches "a macroscale device…which is interfaced with a microfluidic device using double sided tape or transfer tape to form a stable association between the microfluidic device and the macroscale device, wherein the double sided tape comprises a first adhesive surface which associates with the macroscale device and a second adhesive surface which associates with the microfluidic device, wherein the microfluidic device has a plurality of microchannels suitable for containing a fluid stream, and wherein each microchannel comprises an outlet 'for delivering a substantially separate aqueous stream into the sensor chamber,' and at least one sensor." (Office Action, p. 3 - 4). The Examiner argues further that "regarding 'for delivery…sensor chamber,' a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." (Office Action, p.4).

The '179 reference is different from the present invention. The '179 reference is directed to architecture for packaging surface micromachined electro-microfluidic devices. The '179 reference teaches an electromicrofluidic package that can be plugged into a fluidic printed wiring board, and that uses electric and fluidic connections (col 4, lines 36 – 50). According to the '179 reference, "(t)he larger package consists of a circuit board with

embedded fluidic channels and standard fluidic connectors...(and) (t)he embedded channels connect to the smaller package, an Electro-Microfluidic Dual-Inline-Package (EMDIP) that takes fluid to the microfluidic integrated circuit (MIC)." (see, e.g. abstract). The '179 reference teaches fluidic and electrical connections to surface micromachined electro-microfluidic devices, where fluidic connections are made through holes in the EMDIP that coincide with holes extending through the Microfluidic Integrated Circuit (MIC) from back to front that connect to surface micromachined channels on the front of the module. (col 7, line 6).

Applicants point out Figure 21 of the '179 reference. Figure 21 teaches a device that is clearly different from the present invention. Nowhere does Figure 21, or any of the other Figures, show a microfluidic device with three or more microchannels suitable for containing a fluid stream, at least one sensor chamber containing at least one sensor, and where each microchannel comprises an outlet for delivering a substantially separate aqueous stream into the sensor chamber, wherein the outlets of the microchannels intersect with at least one of the sensor chambers, and wherein the microfluidic device comprises a scanning mechanism for selectively exposing a sensor to multiple fluid streams from the three or more microchannel outlets.

Figure 21 shows an "assembly 15 (that) comprises an electro-microfluidic device 100 attached directly to a fluidic printed wiring board (FPWB) 110. An adhesive gasket 26 provides combined mechanical bonding and fluidic coupling between fluidic inlet and outlet ports on the bottom side of device 100 (e.g. ports 101), and fluidic channels 20 and 20' disposed inside of FPWB 110. Assembly 15 can further comprise microcapillary glass tube 120 attached to the backside of FPWB 110 and fluidically coupled to channel 20." (col. 17, line 12).

Nowhere in the '179 reference is there teaching or suggestion that the assembly would be capable of performing the delivery of a separate aqueous stream into the sensor chambers, and wherein the microfluidic device comprises a scanning mechanism for selectively exposing a sensor to multiple fluid streams from the three or more microchannel outlets, as claimed in the present invention.

Nowhere in the description or in any of the figures of the '179 reference is there teaching or suggestion that the microfluidic device, which the Examiner argues is the chip

(100), has a plurality of microchannels suitable for containing a fluid stream; and wherein the microfluidic device has at least one sensor chamber containing at least one sensor, and wherein each microchannel comprises an outlet for delivering a substantially separate aqueous stream into the sensor chambers, and wherein the microfluidic device comprises a scanning mechanism for selectively exposing a sensor to multiple fluid streams from the plurality of microchannel outlets, as taught in the present invention.

The Examiner argues that "Benavides et al. disclose having a sensor but does not explicitly teach that the microfluidic device comprises a scanning mechanism for selectively exposing a sensor to multiple fluid streams from the plurality of microchannel outlets." (Office Action, p.4). The Examiner argues that "Orwar et al. disclose a cell based biosensor which teaches the use of a scanning mechanism (8,17) for selectively exposing a sensor to multiple fluid streams from the plurality of microchannel outlets, as shown in Figure 4A." (Office Action, p.4). The Examiner argues further that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a scanning mechanism for selectively exposing a sensor to multiple fluid streams from the plurality of microchannel outlets as taught by Orwar et al. into the device of Benavides et al. in order to improve the resolution of the detected bioactive analytes (col. 12, lns., 37 – 42)." (Office Action, p.4).

The '303 reference provides methods and apparatus for detection of biologically active analytes separated by liquid based separation means. The Examiner has pointed out Figure 4, shown below:

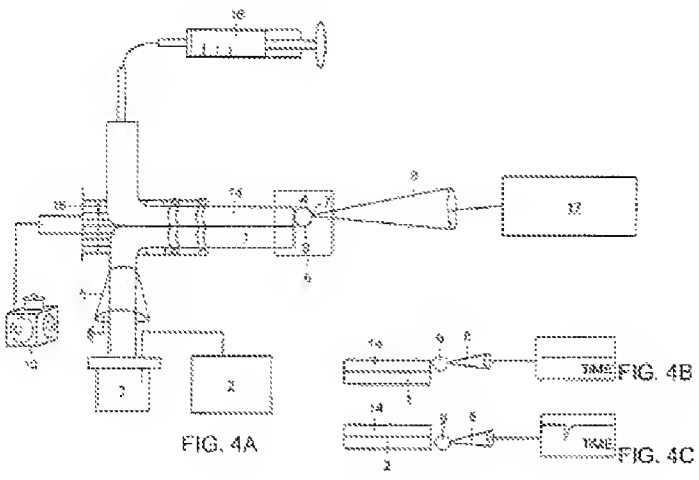

FIG. 4A FIG. 4B FIG. 4C

The Examiner argues that the '303 reference discloses a scanning mechanism for selectively exposing a sensor to multiple fluid streams from a plurality of microchannels; however, as shown in Figure 4, the '303 reference teaches teach **two** fused silica capillaries, where the position of a sensor that is attached to an electrode is placed in front of one of the capillaries and then its position is switched to the second outlet.

> FIGS. 4A-B show a model of a device constructed for switching between superfusion and electrophoresis. FIG. 4A shows the device consisting of two fused silica capillaries which are mounted in parallel. The cell, which is attached to the patch clamp electrode, is placed in front of one of the two capillaries by a micromanipulator. FIG. 4B illustrates how the receptors at the cell-surface are resensitised due to superfusion of the cell by a physiological buffer when the cell is in position one. FIG. 4C illustrates how electrophoretically separated analytes are detected by means of patch clamp when the cell is in position two. (col. 5, lines 34 – 44).

The '303 reference teaches an apparatus with no more than two capillaries. The '303 reference does not teach an scanning mechanism, but rather teaches a method for **switching a position of the first and second capillaries** so that the patch-clamped biosensor alternatively is placed in front of the outlet of the first capillary and in front of the outlet of the second capillary. (see claim 1).

The '303 reference does not cure the flaws of the '179 reference. One of ordinary skill in the art would not be motivated or even able to use the teaching of Orwar, where the

apparatus comprises two fused capillaries and a means for switching a cell between the two capillaries, in the device of the '179 reference.

None of the '621, '199, '766 or '152 references cures the defects of the '179 reference.

The '179 reference provides no teaching or motivation to provide a microfluidic substrate that comprises a plurality of microchannels where each microchannel comprises an outlet for delivering a substantially separate aqueous stream into a sensor chamber, and wherein the microfluic device comprises a scanning mechanism for selectively exposing a sensor to multiple fluid streams from the plurality of microchannel outlets.

As set forth above, the '179 reference features architecture for packaging surface micromachined electro-microfluidic devices. The '179 reference is directed to a need for a standardized electromicrofluidic package that can be plugged into a standard electrical printed circuit board. (col. 4, line 36 – 40). The '179 reference nowhere teaches or suggests microfluidic devices as presently claimed.

None of the '199, '766 or '152 references, when combined with the '179 reference, teaches a system comprising the microfluidic device as claimed.

Accordingly, Applicants request withdrawal of the rejection and allowance of the claims.

Double Patenting

The Examiner argues that if claims 28 and 29 are found allowable, then claims 48 and 49 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. The Examiner argues that "when two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim." (Office Action, p.9). Applicants respectfully traverse the rejection.

The claims are directed to different embodiments, and are not unnecessarily duplicative.

However, in the interest of advancing prosecution, should claims 28 and 29 be allowed, applicants would consider amending or canceling any claims that would be duplicates of the allowed claims under 37 CFR 1.75.

The Examiner argues that claims 28, 29, 48, 49 and 57 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 3 of US Patent No. 7,563,614 (the '614 patent) to Orwar et al. in view of Benavides et al. (the '179 reference, as above). Applicants respectfully disagree.

The Examiner argues that "Orwar et al. '614 disclose a substrate for changing a solution environment around a sensor, the substrate comprising a plurality of microchannels, each microchannel comprising an outlet, and at least one sensor chamber, wherein the outlets of the microchannels intersect with at least one of the sensor chambers, a scanning mechanism for selectively exposing a sensor to multiple fluid streams from the plurality of microchannel outlets." (Office Action, p.13). The Examiner argues that the '614 reference is "silent to having a macroscale device which is interfaced with a microfluidic device using double-sided tape or transfer tape to form a stable association between the microfluidic device and the macroscale device." (Office Action, p.13). The Examiner argues that Benavides et al. disclose "a macroscale device having a tubing outer diameter... which is interfaced with a microfluidic device using double sided tape or transfer tape to form a stable association between the microfluidic device and the macroscale device." (Office Action, p.13). The Examiner argues that "(i)t would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute a macroscale device which is interfaced with a microfluidic device using double-sided tape or transfer tape to form a stable association between the microfluidic device and the macroscale device...wherein the microfluidic device has a plurality of microchannels suitable for containing a fluid stream, and wherein each microchannel comprises an outlet as taught by Benavides et al. with the substrate of Orwar et al." (Office Action, p.14).

As discussed above, Benavides (the '179 reference) is directed to architecture for packaging surface micromachined electro-microfluidic devices. The '179 reference teaches an electromicrofluidic package that can be plugged into a fluidic printed wiring board, and that uses electric and fluidic connections (col 4, lines 36 – 50). According to

the '179 reference "(t)he larger package consists of a circuit board with embedded fluidic channels and standard fluidic connectors...(and) (t)he embedded channels connect to the smaller package, an Electro-Microfluidic Dual-Inline-Package (EMDIP) that takes fluid to the microfluidic integrated circuit (MIC)." (see, e.g. abstract). The '179 reference teaches fluidic and electrical connections to surface micromachined electro-microfluidic devices, where fluidic connections are made through holes in the EMDIP that coincide with holes extending through the Microfluidic Integrated circuit (MIC) from back to front that connect to surface micromachined channels on the front of the module. (col 7, line 6).

Nowhere in the '179 reference is there teaching or suggestion that the assembly would be capable of performing the delivery of a substantially separate aqueous stream into the sensor chambers.

Applicants respectfully request that the rejection be withdrawn.

CONCLUSION

In light of the above remarks, Applicants respectfully request early consideration and allowance of the subject application.

Should the Examiner wish to discuss any of the amendments and/or remarks made herein, the undersigned attorney would appreciate the opportunity to do so.

The Commissioner is hereby authorized to charge any fees that may be required, or credit any overpayment to Deposit Account No. 04-1105.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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